

## **REMARKS**

### **The Specification Amendments**

Applicants have amended the specification to insert a cross-reference to other applications from which the instant application claims benefit of priority.

### **The Claim Amendments**

Applicants have canceled claims 2, 3, and 24 without prejudice.

Applicants have amended claims 5 – 9, 11, 13, 14, 16, 18, 19, 21, and 22 to delete improper multiple dependencies. Applicants have amended claims 1, 4, 10, 14, 17, 22, and 23 to improve their form.

Applicants have amended claim 1, 9, 10, 22, and 25 to replace “plant” or “plant cell” with “*Linum usitatissimum* plant” or “*Linum usitatissimum* cell.” Support for this amendment appears, e.g., in claim 2 as originally filed.

Applicants also have amended claim 1 to recite that the recombinant DNA molecule confers resistance to a first antibiotic and a second antibiotic which is different from the first antibiotic. Support for this amendment appears, e.g., on page 3, lines 16 – 22. Finally, applicants have amended claim 1 to recite that the first and second antibiotics “can be used for selecting a transformed plant cell, a transformed callus or a transformed plant.” Support for this amendment appears, e.g., page 5, lines 9 – 23.

Applicants have amended claims 15 and 16 to include the full chemical names for the abbreviations NAA, TDZ, and BAP at their first occurrence as required by the

Examiner. Applicants have amended claim 23 to recite that the harvestable part or propagation material comprises at least one recombinant DNA molecule.

Applicants have amended claim 25 to recite “a method for the production of male and/or female sterile *Linum usitatissimum* plants, disease-resistant *Linum usitatissimum* plants, *Linum usitatissimum* plants with modified fiber composition or *Linum usitatissimum* plants that tissue-specifically produce specific chemical or biological compounds comprising the method of claim 1.” Support for this amendment appears, e.g., in claim 25 as originally filed.

None of these amendments adds new matter. After entry of the amendments, claims 1, 4 – 23, and 25 will be pending.

#### **The Claim Objections**

The Examiner has objected to claims 4 – 25 under 37 C.F.R. § 175(c) as being improperly multiply dependent. Applicants have amended the claims to remove multiple dependencies, thus obviating the objection.

#### **Priority**

The Examiner indicates that if applicant desires priority based on a previously filed application the specification must contain a specific reference to the earlier filed application(s). Applicants have amended the specification to insert a specific reference to earlier filed applications.

The Examiner also notes that certified copies of the priority documents have not been filed. Applicants have enclosed a certified copy of the European patent application 99114074.0.

### **Drawings**

The Examiner has required new drawings. Specifically, the Examiner indicates that Figures 1 and 2 are not of sufficient quality to permit examination. Applicants have enclosed substitute formal drawings for Figures 1 and 2.

### **The Rejections under 35 U.S.C. § 101**

The Examiner has rejected claims 23 – 25 under 35 U.S.C. § 101 as being directed to non-statutory subject matter. Specifically, the Examiner contends that claim 23 is drawn to plant propagation material that does not necessarily comprise the transgene and that claims 24 – 25 are drawn to a “use.”

Applicants have amended claim 23 to clarify that the plant propagation material comprises the recombinant nucleic acid molecule. Applicants have canceled claim 24 and recast claim 25 as a method claim, thus obviating the rejection with respect to these claims.

### **The Rejections under 35 U.S.C. § 112, First Paragraph**

The Examiner has rejected claims 24 – 25 under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner states that one of skill in the art would not know how to use the claimed invention because of the alleged lack of utility. The amendments

discussed above for the rejection under 35 U.S.C. § 101 obviate this aspect of the rejection under 35 U.S.C. § 112, first paragraph.

The Examiner has rejected claims 1 – 25 under 35 U.S.C. § 112, first paragraph, as lacking enablement. Specifically, the Examiner contends that the specification does not enable a person skilled in the art to use the invention commensurate in scope with the claims. The Examiner states that the claims are drawn to all plants of the genus *Linum*, including linseed, flax and *Linum usitatissimum*; to all explants including leaves, roots, stems, hypocotyls, flowers and seed pods; all culture media; all *Agrobacterium*; all vectors, antibiotics, selective markers; and all plant parts. The Examiner states that plant transformation is generally unpredictable and *Agrobacterium*-mediated transformation of monocots is particularly unpredictable. The Examiner contends that in view of this unpredictability it would require undue experimentation to determine all of the conditions necessary to accomplish the claimed method. Applicants traverse in view of the amendments to the claims.

Applicants have amended claim 1 to recite transformation of a plant cell from the species *Linum usitatissimum*. Contrary to the Examiner's assertion, transformation of *Linum usitatissimum* was not unpredictable at the time the instant application was filed. Indeed, methods for transforming *Linum usitatissimum* were well-known in the art. See, e.g., Bretagne-Sagnard et al., "Selection of transgenic flax plants is facilitated by spectinomycin," *Transgenic Research* 5:131-37 (1996) (Bretagne-Sagnard), which was cited by the Examiner. Accordingly, applicants need not provide detailed descriptions relating to

the selection of culture media, *Agrobacterium* strains, etc., because these were all well-known to one of ordinary skill in the art at the time the instant application was filed.

However, transformation of *Linum usitatissimum* using the available methods was unsatisfactory both because these methods were extremely inefficient and because they typically produced plants with morphological and/or physiological abnormalities. Applicants claimed method is vastly superior to these methods. For example, applicants' method has an approximately 80% success rate (Example 3) as compared to 15% in Bretagne-Sagnard (page 136, left col., last paragraph) and plants obtained using the methods of the invention are fertile and phenotypically normal.

Applicants' invention is based on the surprising discovery that this vast improvement in transformation can be obtained by utilizing two different antibiotics for selection of transformed plants. See, e.g., page 3, lines 8 – 12 and 21 – 22. Accordingly, applicants have specifically exemplified the transformation according to the methods of the invention of the *Linum usitatissimum* flax variety Flanders with four very different binary vectors (JH5, pPZPHV5, pJH7, and pHLHVO) comprising different combinations of single or paired selective markers. See, e.g., Examples 3 – 6, specification pages 23 – 28. In addition, the specification teaches a large number of selectable markers and their corresponding antibiotics as well as scorable markers that may be used in the methods of the invention. See, e.g., page 5, lines 9 – 23; page 13, line 23 to page 14, line 13. Thus, contrary to the Examiner's assertions, the specification teaches a person of ordinary skill in the art how to use the invention commensurate in scope with the amended claims.

**The Rejections under 35 U.S.C. § 112, Second Paragraph**

The Examiner has rejected claims 1 – 25 under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Examiner contends that claim 1 lacks agreement between the preamble and the method steps and states that the method steps are not in proper order. Applicants have amended claim 1 as suggested by the Examiner, thus obviating the rejection.

The Examiner also states that the abbreviations or acronyms recited in claims 15 – 17 must be spelled out at least once. Applicants have amended claims 15 – 17 to spell out the abbreviations NAA, TDZ, and BAP at their first occurrence as required by the Examiner.

**The Rejection under 35 U.S.C. § 102**

The Examiner has rejected claims 1 – 5, 7 – 9, 11, 13 – 25 under 35 U.S.C. § 102(b) as being anticipated by Bretagne-Sagnard. Specifically, the Examiner states that Bretagne-Sagnard teaches a method for generating transgenic *Linum* plants comprising introducing a recombinant DNA binary vector comprising a selectable marker which confers resistance to at least one antibiotic (kanamycin) into hypocotyl cells of a flax plant, induction of transgenic callus and regenerating transgenic flax plants after culturing the calli on a medium containing a different second antibiotic (cefotaxime). The Examiner states that Bretagne-Sagnard also teaches introduction of a selectable marker gene operably linked to expression control regions by *Agrobacterium*, a medium containing the first antibiotic, NAA and TDZ or BAP, a medium containing the second antibiotic that is free of auxins or

cytokinins, a DNA encoding the scorable marker GUS, and transgenic plant cells, callus, tissues or plants. Applicants traverse in view of the claims, as amended.

As described above, applicants have amended claim 1 to recite that the recombinant DNA molecule comprises selectable marker(s) that confer resistance to at least a first antibiotic and to a second antibiotic which is different from said first antibiotic. In addition, applicants have amended claim 1 to recite that said first antibiotic and said second antibiotic can be used for selecting a transformed plant cell, a transformed callus or a transformed plant. Accordingly, it is clear that the two antibiotics recited in the amended claims must be active in plants and that they are used in the methods of the invention to select for resistant plants.

In contrast, the second antibiotic used by Bretagne-Sagnard, cefotaxime, is an inhibitor of bacterial cell wall synthesis. Thus, cefotaxime is not active in plants. Consistent with this, Bretagne-Sagnard indicates that cefotaxime is used to eliminate *Agrobacterium*. See, e.g., page 132, right column, beginning of section entitled "Selection and regeneration." Accordingly, Bretagne-Sagnard does not anticipate the amended claims.

#### **The Rejection under 35 U.S.C. § 103**

The Examiner has rejected claims 1 – 9 and 11 – 25 under 35 U.S.C. § 103(a) as unpatentable over Bretagne-Sagnard in view of Stachel et al., "Identification of the signal molecules produced by wounded plant cells that activate T-DNA transfer in *Agrobacterium tumefaciens*," *Nature* 318:624-29 (1985) (Stachel). Specifically, the Examiner acknowledges that Bretagne-Sagnard does not teach the use of kanamycin as the

first antibiotic and G-418 as the second antibiotic. However, the Examiner states that Bretagne-Sagnard does teach the use of G-418 as a selective agent and contends that it is well known that G-418 may be used as an alternative to kanamycin. The Examiner contends that it would have been obvious to one of skill in the art to substitute a different antibiotic for the cefotaxime used in Bretagne-Sagnard. Furthermore, the Examiner also acknowledges that Bretagne-Sagnard does not teach the presence of acetosyringone with the *Agrobacterium*, but contends that Stachel teaches that acetosyringone activated T-DNA transfer from *Agrobacterium* and that its use would be obvious to one of skill in the art. Finally, the Examiner contends that using synchronized germinating seed is mere optimization, which would be obvious to one of skill in the art. Applicants traverse.

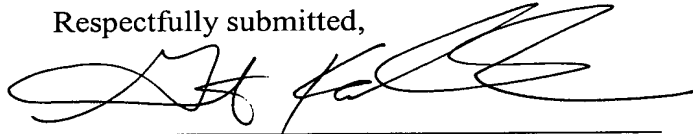
As discussed above, the two antibiotics recited in the amended claims must be active in plants and they are used in the methods of the invention to select for resistant plants. In contrast, Bretagne-Sagnard uses a second antibiotic only to eliminate *Agrobacterium*. Nowhere do either Bretagne-Sagnard nor Stachel teach or suggest the use of two separate antibiotics for the selection of transformed *Linum usitatissimum* plants. Accordingly, these references, either alone or taken together, do not render the amended claims obvious.



**Conclusion**

For the reasons presented above, applicants request that the Examiner allow claims 1, 4 – 23, and 25 to issue.

Respectfully submitted,



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